An updated sequence listing indicating the changes commensurate in scope with the changes in the table is included herein.

Rejections under 35 U.S.C. § 112

Claim 4 has been rejected under 35 U.S.C. § 112, second paragraph as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Applicants respectfully traverse.

The Examiner argues that the ordinary artisan would not know what is meant by "replaced by one or a pair of replacement primers." According to the Examiner the specification does not disclose what is intended by a replacement primer, therefore, the metes and bounds of the instant invention are undefined. Applicants respectfully disagree. The specification on pages 4-5 explicitly explain what is meant by a replacement primer and in Table 2, pages 12-13, the specification provides a list of replacement primers. Thus, the skilled artisan, armed with the specification, would be able to clearly determine the metes and bounds of the instant invention and the Applicants respectfully request that this rejection be withdrawn.

Claims 1, 2, 5, 6 and 7 were rejected under 35 U.S.C. § 112, second paragraph as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Applicants respectfully traverse. The Examiner contends that the phrase "as represented in" is unclear. In an effort to expedite prosecution, the Applicants have amended the claims to replace "as represented in" with the phrase "chosen from." Thus, Applicants respectfully request that this rejection be withdrawn.

Rejections under 35 U.S.C. § 103

Claims 1-8 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Hertogs et al in view of any one of Zazzi et al, Kozal et al., Birk et al., Cabana et al., or Boden et al. Applicants respectfully traverse.

The Examiner argues that Hertogs et al teaches a method of detecting phenotypic resistance with mutation in the HIV pol gene starting with an isolated virus including using a nested PCR method using the outer primer sequence SEQ ID NO 1 and 2 of the present invention, and a secondary primer. The Examiner admits, however, that the reference does not teach the sequences disclosed in SEQ ID No. 3-12. The Examiner similarly relies on of Zazzi et al, Kozal et al., Birk et al., Cabana et al., or Boden et al. for the teaching of a nested PCR method using inner and outer primes as well as sequencing primers for the determination of the HIV-1 pol genotype. As the Examiner admits, none of these references disclose SEQ ID Nos. 3-12. Instead, the Examiner argues that SEQ ID Nos. 3-12 are the functional equivalents of the sequences disclosed in the prior art.

The Examiner's argument, however, is missing a fundamental premise. To establish a *prima facie* case of obviousness, the prior art reference or references must teach or suggest all the claim limitations. See M.P.E.P. § 2143. Thus, while the Office may in some cases rely on functional equivalence as a rationale supporting an obviousness rejection under M.P.E.P. § 2144.06, the Office is still required to demonstrate that the species is known in the art for some other purpose. Functional equivalence may merely provide the Examiner with a rationale for using a known species in the claimed invention. Since the Examiner has not provided a prior art reference that discloses the specific primers of SEQ ID NO: 3-12 and has even admitted that the specific primers disclosed in SEQ ID NO: 3-12 are not taught in the prior art (See Official Action, page 7. "although the prior art does not teach the

specific primers disclosed in SEQ ID NO: 3-12."), the Examiner can not rely on functional equivalence to support an obviousness rejection.

Even assuming arguendo that the Examiner did find the specific primers disclosed in SEQ ID Nos: 3-12 in the prior art, the combination of primers claimed in the present invention demonstrates that the sequences of the prior art are not functional equivalents and that the combination of sequences of the present invention provides unexpected results. The Examiner's argument is based on his characterization of Hertogs et al. which states "[t]he advantage of the Hertogs primer is that it amplifies a **large region** of the HIV-a gene providing a larger template to be subjected to the secondary primers allowing for the sequencing of more areas **known** to contain mutations after drug treatment. See Official Action, page 6 (emphasis added). The combination of sequences of the present invention, however, unexpectedly allows the skilled artisan to genotype **any** mutation, not just those mutations known in the art, and provides the ability to genotype a much broader range of RT, *e.g.*, up to 400 amino acids, than the cited references, including Hertogs et al.

In summary, the contention that the sequences of the prior art are functional equivalents of SEQ ID Nos. 3-12 is insufficient to establish obviousness for at least the reason the prior art does not teach or suggest the specific primers of SEQ ID NO: 3-12. Moreover, the clamed combination of sequences provides the unexpected result of genotyping any mutation and genotyping a much broader range of RT. For at least these reasons, Applicants respectfully request that this rejection be withdrawn.

Claims 1 and 9 were also rejected under 35 U.S.C. § 103(a) as being unpatentable over Hertogs et al in view of Demeter et al. Applicants respectfully

traverse. Demeter et al does not correct the deficiencies of Hertogs et al described above. More specifically, since the Examiner has not provided a reference which discloses the primers of SEQ ID Nos. 3-12, the prior art references relied on do not teach or suggest all the claim limitations as required by the M.P.E.P. Additionally, the claimed combination of sequences provides the unexpected beneficial result of genotyping any mutation and genotyping a much broader range of RT than the prior art sequences. Applicants respectfully request that this rejection be withdrawn.

Please grant any extensions of time required to enter this response and charge any additional required fees to our deposit account 06-0916.

Respectfully submitted,

FINNEGAN, HENDERSON, FARABOW,
GARRETT & DUNNER, L.L.P.

Dated: May 24, 2002

By: _____
Anthony C. Tridico
Reg. No. 45,958

APPENDIX TO THE RESPONSE AND AMENDMENT

Amendments to Claims

1 . A method for detection of mutations in the *pol* gene of HIV-1 isolates comprising the steps of:

a) isolation of a sample comprising HIV-1 RNA,

b) PCR amplifying RNA from said sample using a primer chosen from an outer primer **chosen from** [as represented in] SEQ ID No: 1 [and] **or SEQ ID No:** 2 to obtain a primary PCR product,

c) PCR amplifying said primary PCR product using a 5' and 3' primer chosen from an inner primer **chosen from** [as represented in] SEQ ID No: 3, **SEQ ID No:** 4, **SEQ ID No:** 5 [and] **or SEQ ID No:** 6 to obtain a secondary PCR product, and

d) sequencing said secondary PCR product.

2. A method according to Claim 1, wherein said secondary PCR product is sequenced using at least one sequencing primer chosen from [primers as represented in] SEQ ID No: 7 [to 12] **SEQ ID No: 8, SEQ ID No: 9, SEQ ID No: 10, SEQ ID No: 11, or SEQ ID No: 12**.

4. A method according to Claim [2] **1**, **wherein said secondary PCR product is sequenced using at least one sequencing primer chosen from SEQ ID No: 7 SEQ ID No: 8, SEQ ID No: 9, SEQ ID No: 10, SEQ ID No: 11, or SEQ ID No: 12 and**

wherein at least one of said sequencing primer is replaced by one or a pair of replacement primers.

5. A method according to Claim 1, wherein said secondary PCR product is sequenced using at least one sequencing primer chosen from primers up to 1, 2, 3 or 4 nucleotides upstream or downstream primer regions [as represented in SEQ ID No: 7 to 12] **chosen from SEQ ID No: 7, SEQ ID No: 8, SEQ ID No: 9, SEQ ID No: 10, SEQ ID No: 11, or SEQ ID No: 12**.

6. A method according to Claim 1, wherein the outer primer is chosen from primers up to 1, 2, 3 or 4 nucleotides upstream or downstream primer regions [as represented in] **chosen from** SEQ ID No: 1 [and] **or SEQ ID No:**2.

7. A method according to Claim 1, wherein the inner primer is chosen from primers up to 1, 2, 3 or 4 nucleotides upstream or downstream primer regions [as represented in] **chosen from** SEQ ID No: 3, **SEQ ID No:** 4, **SEQ ID No:** 5 [and] **or SEQ ID No:** 6.